BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

EXPRESS MAIL CERTIFICATE

Date_____ Label No._____

I hereby certify that, on the date indicated above, this paper or fee was deposited with the U.S. Postal Service & that it was addressed for delivery to Mail Stop Non-Fee Amendments, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 by AExpress Mail Post Office to Addressee@ service.

_____ _____

Name (Print) Signature

PLEASE CHARGE ANY DEFICIENCY UP TO $300.00 OR CREDIT ANY EXCESS IN THE FEES DUE WITH THIS DOCUMENT TO OUR DEPOSIT ACCOUNT NO. 04-0100

Customer No.: **07278**

Docket No: 03394/100H557-US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Ehud Goldin et al.

Serial No.: 09/851,494 Art Unit: 1646

Confirmation No.:

Filed: Examiner: John D. Ulm

For: **Gene Encoding A New TRP Channel Is Mutated In Mucolipodosis IV**

DECLARATION UNDER 37 C.F.R. § 1.131

Mail Stop Non-Fee Amendments
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Susan A. Slaugenhaupt, hereby declare and state as follows:

1. I am a citizen of the United States of America. I am more than twenty-one years of age.

2. I am a co-inventor of the above-identified application, along with James S. Acierno JR. James S. Acierno JR and I did the work that resulted in the data reported in the declaration, or it was done under my supervision as head of the laboratory.

3. I make this statement on behalf of myself and the co-inventors identified in paragraph 2.

4. I reaffirm my duty of candor and good faith in dealing with the Office, including the duty to disclose to the Office all information known to be material to the patentability of the invention as defined in 37 C.F.R. § 1.56.

5. I have read and am familiar with the instant application as it was filed in the U.S. Patent and Trademark Office.

6. I have read and am familiar with the publications by (i) Curtis et al. (Pub. No. US 2002/0035056 A1), which has an effective filing date under 35 U.S.C. 119(e) of Apr. 07, 2000; and (ii) Lal et al. (Pub. No. US 2002/0182671 A1), which has an effective filing date under 35 U.S.C. 119(e) of Aug. 17, 1999.

7. It is my understanding that, according to the Examiner, the amino acid sequence presented in SEQ ID NO: 3 of the instant application is identical to the amino acid sequence presented in SEQ ID NO: 2 of Curtis et al. and SEQ ID NO: 13 of Lal et al. It is further my understanding, that the Examiner states that Curtis et al. and Lal et al. each present an isolated nucleic acid encoding a protein comprising the amino acid sequence presented in

SEQ ID NO: 3 of the instant application, as well as a vector and host cell comprising that nucleic acid.

8. Prior to Aug. 17, 1999, the effective date of the Lal et al. publication, we conceived and reduced to practice the invention as described and claimed in claims 1, 5-7, and 33-34 of the subject application.

9. As evidence that our reduction to practice antedates Lal et al., we refer to Exhibits 1 and 2, which collectively establish the conception and reduction to practice of our invention prior to Aug 17, 1999. The exhibits document isolation and possession of a nucleic acid encoding MCOLN1 prior to Aug. 17, 1999. Dates, along with privileged information, appearing in these documents have been redacted, but each document has a date before August 17, 1999.

10. Exhibit 1 establishes identification of MCOLN1 sequence, showing the receipt by Dr. Slaugenhaupt of two primers: (i) sts-T66288-R (5'-AGC TGC AGG CCT ACA TCG -3'); and (ii) sts-T66288-F (5'GGC AGT CAG GTC GAA TCA AT-3). As shown in Appendix A, the two primers are specific to the MCOLN1 gene, spanning the 1732-1883 bp region of the MCOLN1 cDNA sequence (SEQ ID NO: 3).

11. Exhibit 2 documents identification and possession of a nucleic acid encoding a full-length MCOLN1 protein by showing an EST alignment spanning the MCOLN1 gene. At least two notations are particularly relevant. First, this page shows a "2264 bp"

annotation of T66288 following sequencing, indicating that T66288 encodes the entire MCOLN protein. Prior to our sequencing, the exact insert size of this construct was not known. Second, this page also identifies the orientation of AI8166064, which is the corresponding GenBank accession number for IMAGE CLONE 2517653 (Appendix B). Paragraph [0185] of the specification states that we "sequenced the IMAGE clone 2517653." This paragraph further describes our deduction and confirmation of the MG-2 (MCOLN) open-reading frame from this clone.

12. With the isolation and identification of the MCOLN1 coding region, we also achieved reduction to practice of an expression vector encoding the MCOLN1 protein prior to August 17, 1999. Appendix B reveals that IMAGE CLONE 2517653 (as presented in Exhibit 2) is inserted into the pBlusescript SK+ vector. This common vector is widely recognized by those skilled in the art of molecular biology as including T3 and T7 promoters that flank the cloning site, which allow expression of the inserted gene sequence. Appendix C shows the key structural features of this vector. The entire MCOLN1 open reading frame is present in IMAGE CLONE 2517653. Alternatively, given our identification of the coding sequence of MCOLN1, we knew how to incorporate that sequence into an expression vector such as pBluescript SK+.

13. These documents establish that the inventions of claims 1, 5-7, and 33-34 were reduced to practice prior to Aug. 17, 1999.

14. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true. I

further declare that these statements are made with the knowledge that the willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United Stated Code, and that such willful false statements may jeopardize the validity of the instant application or of any patent issued thereupon.

Respectfully submitted,

6/21/04
DATE

Susan A. Slaugenhaupt
Susan A. Slaugenhaupt

EXHIBIT A - PAGE 1

IDT®

Integrated DNA Technologies, Inc.

Oligonucleotide Specification Sheet

1710 Commercial Park
Coralville, IA 52241
Phone: 800-328-2661
Fax: 319-626-8444
E-Mail: orders@idtdna.com
http://www.idtdna.com

Customer Information

Susan Slaugenhaupt
Harvard Institute of Human Genetics
Massachusetts General Hospital-Boston
77 Avenue Louis Pasteur HIM Bldg. Rm. 422
Boston, MA 02115
6174327025

Order Information

Order Date : [redacted]
Customer # : 19479
P.O. # : 0000085288

Sales order # : 148396
Reference #: 624757

Oligonucleotide Information

Reference # : **624757**
Purification : **Standard Purification**
Sequence Name : **sts-T66288-f**

Product : **DNA Oligo Sample**
Unit Size : **100 nmole**
Bases : **20**

Sequence : **5'- GGC AGT CAG GTC GAA TCA AT -3'**

10 x 4 = 40
10 x 2 = 20
60

Molecular Weight :	7,572.00
GC Content :	50.0 %
Tm (50mM NaCl) :	51.44 °C

Amount of Oligo				
21.8	=	95.01	=	0.72
OD_{260}		nanomoles		mg

Printed 6/9/99

1569

LABELS - PEEL HERE

624757 Integrated DNA Tech
S. Slaugenhaupt 06/09/99
sts-T66288-f
5'-GGC AGT CAG GTC GAA TCA AT -3'
Tm = 51.44 °C, MW = 7572
21.80 OD_{260} = 95.01 nmol = 0.72 mg

624757 Integrated DNA Tech
S. Slaugenhaupt 06/09/99
sts-T66288-f
5'-GGC AGT CAG GTC GAA TCA AT -3'
Tm = 51.44 °C, MW = 7572
21.80 OD_{260} = 95.01 nmol = 0.72 mg

Samples Statistically Tested

Q.C. Approved By:

PLEASE READ BEFORE OPENING TUBES

* Store at -20°C. If the oligo is to be used on multiple occasions, resuspend in water or tris-EDTA buffer, divide into smaller aliquots, lyophilize, and store at -20°C.
* Contents may appear as either a translucent film or a white powder. This variance does not affect the quality of the oligo.
* Please centrifuge tubes prior to opening. Some of the product may have been dislodged during shipping.
* Calculations are made using 1 OD_{260} = 33 ug / mL

(1) EXHIBIT A (1) PAGE 2

IDT®

Integrated DNA Technologies, Inc.

1710 Commercial Park
Coralville, IA 52241
Phone: 800.328.2661
Fax: 319.626.8444
E-Mail: orders@idtdna.com
http://www.idtdna.com

Oligonucleotide Specification Sheet

Customer Information

Susan Slaugenhaupt
Harvard Institute of Human Genetics
Massachusetts General Hospital-Boston
77 Avenue Louis Pasteur HIM Bldg. Rm. 422
Boston, MA 02115
6174327025

Order Information

Order Date : [redacted]
Customer #: 19479
P.O. # : 0000085288

Sales order # : 148396
Reference #: 624758

Oligonucleotide Information

Reference # : **624758**
Purification : **Standard Purification**
Sequence Name : **sts-T66288-R**

Product : **DNA Oligo Sample**
Unit Size : **100 nmole**
Bases : **18**

Sequence : **5'- AGC TGC AGG GCT ACA TCG -3'**

11x4 = 44
7x2 = 14
58

Molecular Weight :	6,754.00
GC Content :	61.1 %
Tm (50mM NaCl) :	51.11 °C

Amount of Oligo				
15.5	=	75.73	=	0.51
OD_{260}		nanomoles		mg

Printed 6/9/99

1570

LABELS - PEEL HERE

624758 Integrated DNA Tech
S. Slaugenhaupt 06/09/99
sts-T66288-R
5'-AGC TGC AGG GCT ACA TCG -3'
Tm = 51.11 °C, MW = 6754
15.50 OD_{260} = 75.73 nmol = 0.51 mg

624758 Integrated DNA Tech
S. Slaugenhaupt 06/09/99
sts-T66288-R
5'-AGC TGC AGG GCT ACA TCG -3'
Tm = 51.11 °C, MW = 6754
15.50 OD_{260} = 75.73 nmol = 0.51 mg

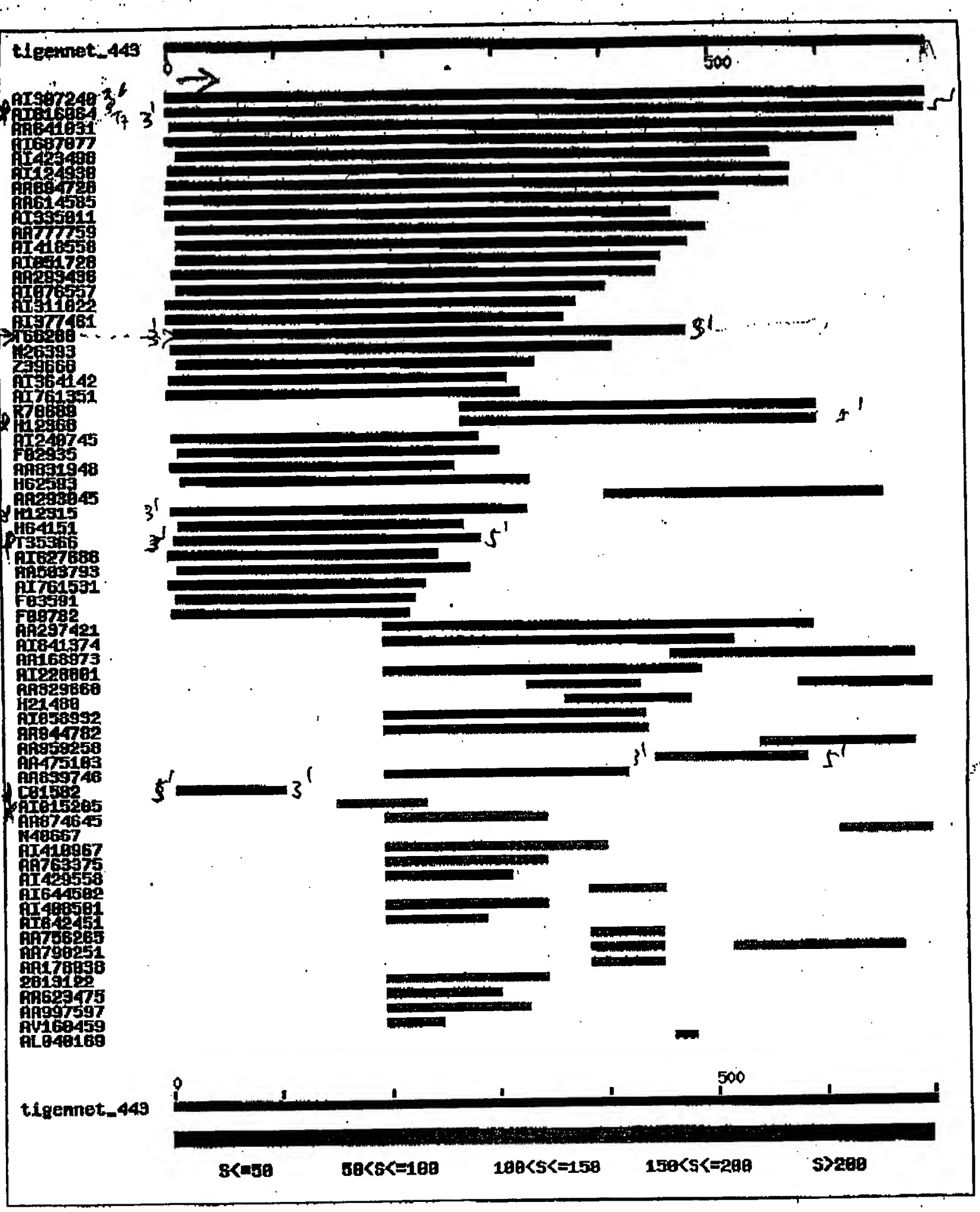
Samples Statistically Tested

Q.C. Approved By:

PLEASE READ BEFORE OPENING TUBES

* Store at -20°C. If the oligo is to be used on multiple occasions, resuspend in water or tris-EDTA buffer, divide into smaller aliquots, lyophilize, and store at -20°C.
* Contents may appear as either a translucent film or a white powder. This variance does not affect the quality of the oligo.
* Please centrifuge tubes prior to opening. Some of the product may have been dislodged during shipping.
* Calculations are made using 1 OD_{260} = 33 ug / mL

EXHIBIT B


tigennet_443
0
500
AI307240
AI816064
AA641031
AI687077
AI423498
AI124930
AA884720
AA614585
AI335811
AA777759
AI418558
AI851728
AA293496
AI876557
AI311822
AI377461
R66288
M26393
Z39668
AI364142
AI761351
R70669
M12368
AI240745
F02935
AA831948
H62583
AA293045
M12315
H64151
T35366
AI627686
AA503793
AI761531
F03591
F08782
AA297421
AI841374
AA168973
AI228861
AA829660
H21480
AI858932
AA844782
AA959258
AA475183
AA839746
C01582
AI815205
AA874645
N48667
AI410967
AA763375
AI429558
AI644582
AI488581
AI842451
AA756265
AA790251
AA178838
2613122
AA623475
AA997597
AV160459
AL048169
tigennet_443
S<=50
50<S<=100
100<S<=150
150<S<=200
S>200

SEQ ID NO: 2

<400> 2
-------- sts-T66288-f
-------- sts-T66288-r

agatcagctg atgccggagg gtttgaagcc gcgccgcgag ggagcgaggt cgcagtgaca 60

gcggcgggcg atcggaccca ggctgccccg ccgtacccgc ctgcgtcccg cgctcccgcc 120

ccagcatgac agccccggcg ggtccgcgcg gctcagagac cgagcggctt ctgaccccca 180

accccgggta tgggacccag gcggggcctt caccggcccc tccgacaccc ccagaagagg 240

aagaccttcg ccgtcgtctc aaatactttt tcatgagtcc ctgcgacaag tttcgagcca 300

agggccgcaa gccctgcaag ctgatgctgc aagtggtcaa gatcctggtg gtcacggtgc 360

agctcatcct gtttgggctc agtaatcagc tggctgtgac attccgggaa gagaacacca 420

tcgccttccg acacctcttc ctgctgggct actcggacgg agcggatgac accttcgcag 480

cctacacgcg ggagcagctg taccaggcca tcttccatgc tgtggaccag tacctggcgt 540

tgcctgacgt gtcactgggc cggtatgcgt atgtccgtgg tgggggtgac ccttggacca 600

atggctcagg gcttgctctc tgccagcggt actaccaccg aggccacgtg gacccggcca 660

acgacacatt tgacattgat ccgatggtgg ttactgactg catccaggtg gatccccccg 720

agcggccccc tccgcccccc agcgacgatc tcaccctctt ggaaagcagc tccagttaca 780

agaacctcac gctcaaattc cacaagctgg tcaatgtcac catccacttc cggctgaaga 840

ccattaacct ccagagcctc atcaataatg agatcccgga ctgctatacc ttcagcgtcc 900

tgatcacgtt tgacaacaaa gcacacagtg ggcggatccc catcagcctg gagacccagg 960

cccacatcca ggagtgtaag caccccagtg tcttccagca cggagacaac agcttccggc 1020

tcctgtttga cgtggtggtc atcctcacct gctccctgtc cttcctcctc tgcgcccgct 1080

cactccttcg aggcttcctg ctgcagaacg agtttgtggg gttcatgtgg cggcagcggg 1140

gacgggtcat cagcctgtgg gagcggctgg aatttgtcaa tggctggtac atcctgctcg 1200

tcaccagcga tgtgctcacc atctcgggca ccatcatgaa gatcggcatc gaggccaaga 1260

acttggcgag ctacgacgtc tgcagcatcc tcctgggcac ctcgacgctg ctggtgtggg 1320

tgggcgtgat ccgctacctg accttcttcc acaactacaa tatcctcatc gccacactgc 1380

gggtggccct gcccagcgtc atgcgcttct gctgctgcgt ggctgtcatc tacctgggct 1440

actgcttctg tggctggatc gtgctggggc cctatcatgt gaagttccgc tcactctcca 1500

tggtgtctga gtgcctgttc tcgctcatca atggggacga catgtttgtg acgttcgccg 1560

ccatgcaggc gcagcagggc cgcagcagcc tggtgtggct cttctcccag ctctaccttt 1620

actccttcat cagcctcttc atctacatgg tgctcagcct cttcatcgcg ctcatcaccg 1680

gcgcctacga caccatcaag catcccggcg gcgcaggcgc agaggagagc g**agctgcagg** 1740

cctacatcgc acagtgccag gacagcccca cctccggcaa gttccgccgc gggagcggct 1800

cggcctgcag ccttctctgc tgctgcggaa gggacccctc ggaggagcat tcgctgctgg 1860

tga**attgatt cgacctgact gcc**gttggac cgtaggccct ggactgcaga gacccccgcc 1920

cccgaccccg cttatttatt tgtagggttt gcttttaagg atcggctccc tgtcgcgccc 1980

gaggagggcc tggacctttc gtgtcggacc cttgggggcg gggagactgg gtggggaggg 2040

tgttgaataa a 2051

APPENDIX B

Biology & Biotechnology Research PROGRAM

The I.M.A.G.E. Consortium

"Sharing resources to achieve a common goal - the discovery of all genes "

Begin new search | Begin new Clone search

I.M.A.G.E. Clone Query Results:

Your search returned **2** results! Here they are:

Result Number	CLONE ID	ROW POS	COL POS	PLATE	GB ACCNUM	SEQ LENGTH	GB DATE CREATED	DATE MODIFIED	CDNA LIBR ID	SPECIES	TISSUE TYPE	VECTOR NAME
1	2517653	1	6	6268	AI815981	448	Jul 09 1999 12:00AM	Apr 17 2003 05:06PM	1341	human	brain/CNS	pBluescript SK+
2	2517653	1	6	6268	AI816064	706	Jul 09 1999 12:00AM	Apr 17 2003 05:06PM	1341	human	brain/CNS	pBluescript SK+

Begin new search | Begin new Clone search

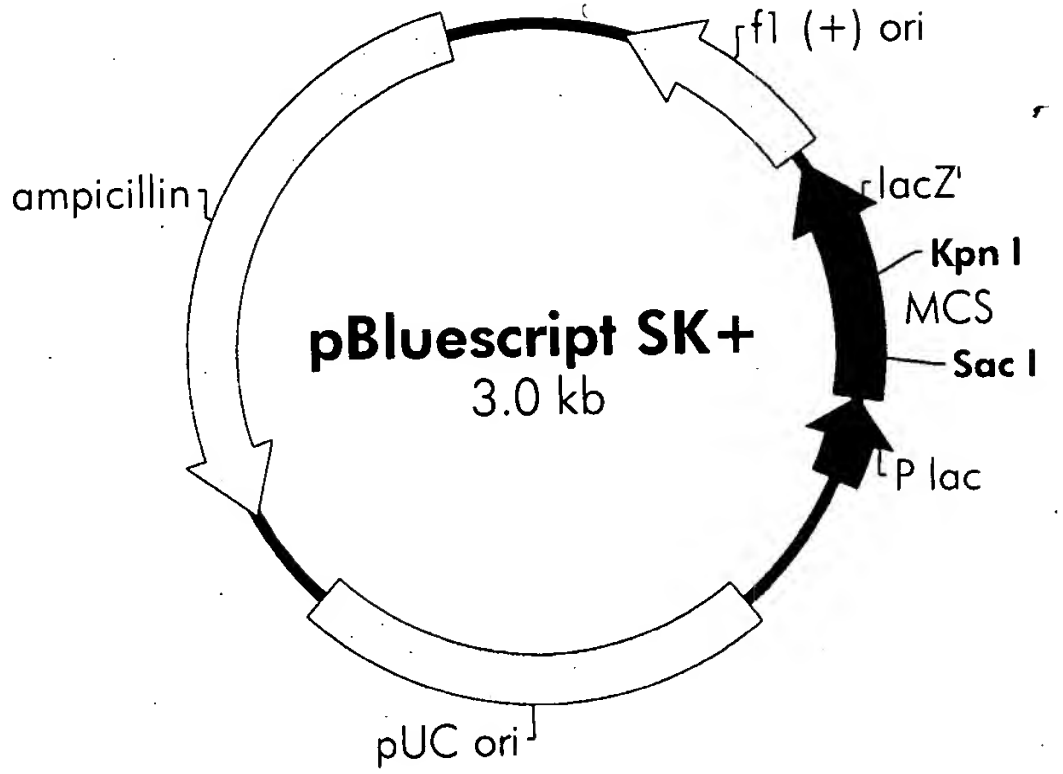
I.M.A.G.E. Consortium home page

BBRP home page

LLNL Programs, Projects, Centers and Consortia

APPENDIX C

f1 (+) origin 138–444
β-galactosidase α-fragment 463–816
multiple cloning site 653–760
***lac* promoter 817–938**
pUC origin 1158–1825
ampicillin resistance (*bla*) ORF 1976–2833



pBluescript SK (+/–) Multiple Cloning Site Region (sequence shown 601–826)